Chapter 7

Genetic Testing and the Prevention of Coronary Heart Disease: A Case Study

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A 50 year-old man, Mr. C, calls the Department of Public Health with a question:

"Will a **genomic profile** *test help me know what I should do to prevent coronary heart disease?"*

Mr. C says that his father had a heart attack when he was 59 years old. He knows that he needs to take care of his health and just had a complete physical, including an electrocardiogram and a treadmill test. Everything checked out fine, but because his cholesterol was "a little high," his doctor recommended a reduced-fat diet and prescribed a lipid-lowering drug. Mr. C's wife then asked her doctor, an alternative medicine practitioner, for another opinion. He suggested that Mr. C should look into the new DNA tests that provide an individualized "genomic profile" and personalized recommendations for nutritional supplements to prevent coronary heart disease. Mr. C visited several Web sites that offer such tests, but wasn't sure whether he should get one. He called the health department because he was looking for an objective opinion, unbiased by provider preferences or commercial interests.

Genomic Profiling
Concurrent detection of multiple gene variants that have been associated with predisposition to a particular disease.

Is Genomic Profiling for Coronary Heart Disease (CHD) Ready for Prime Time?

Diseases of the heart are the leading cause of death in the United States, accounting for almost one third of all deaths. Most of these are due to CHD, including deaths from myocardial infarction and CHD-related heart failure. After declining substantially during the 20th century, CHD and stroke incidence and mortality may be leveling off, suggesting the need not only for redoubled efforts but also for modified strategies to promote healthy lifestyles and improve early detection and intervention.[1]

Mr. C turned 50 in 2003, the year that also marked the 50th anniversary of the discovery of DNA and completion of the Human Genome Project. Sequencing the genome ahead of schedule has further heightened expectations that health benefits will follow quickly. In particular, the idea that genetic tests could offer

people individualized estimates of risk and interventions based on their genotypes has captured the imagination of scientists and the public. This enthusiasm for personalized medicine has fueled a rush to develop and market new genomic tests, often without establishing that the tests are valid or useful.
Several commercial enterprises have sprung up to offer DNA-based tests for susceptibility to complex diseases, with names such as Obesity Susceptibility Profile, Nutritionscreen, Oxidative Stress Profile and CardioGenomic Profile.* These tests are advertised on Web sites that offer extensive information targeted to consumers, as well as information for health care providers. These "genomic profiles" typically consist of tests for combinations of gene variants; the specific combinations are considered proprietary and are usually not disclosed in online or printed product information.

A critical evaluation of genomic profiling for guiding individualized health promotion and disease prevention concluded that this approach is "not ready for prime time" because of lack of evidence in two key areas: [2]

1. **Clinical Validity:** Many initial reports associating one or more genetic variants with coronary heart disease are not confirmed—and are sometimes contradicted—by subsequent research studies. Systematic approaches to reviewing the evidence are still in early stages of development.

2. **Clinical Utility:** Does genomic profiling provide any information that would change individual prevention or management recommendations? Do these recommendations result in positive behavior change and reduced morbidity and mortality?

Medical Family History as Genomic Profiling

An established approach to "genomic profiling" that should not be overlooked is the medical family history. The tendency for coronary heart disease (CHD) to cluster in families was first recognized over one hundred years ago. A positive family history can capture the effects and interactions of shared genetic and environmental factors, whether measured or unmeasured, that lead to disease expression in a family: *"it is quite possible that even with our ability to measure hundreds and thousands of genes and environments we may find that family history is the best, low-cost way to identify the at-risk subgroups in the population."* [3] In this respect, family history is as relevant to public health programs as it is to clinical practice.[4, 5]

*Use of trade names is for example only and does not imply endorsement of DHHS. For examples, see Genovations: Predictive Genomics for Personalized Medicine, http://www.genovations.com; Sciona, http://www.sciona.com; GeneLink: Genetic Biosciences for Improving the Quality of Life, http://www.bankdna.com.

Family History is Still the Best Genomic Tool

In 2002, a meeting on genomics and chronic disease, conducted by the Chronic Disease Directors, a national organization affiliated with the Association of State and Territorial Health Officials, called for investigating the utility of targeting interventions to persons at risk for chronic diseases because of their family history.[6] The meeting report called for extending the use of family history beyond high-risk families to the much larger group of families at moderate risk for chronic disease due to shared genetic background and environment. This interest spurred the development of the Family History Initiative. See *Chapter 6, The Family History Public Health Initiative*, for more information.

Guidelines for CHD Prevention

Public health agencies and medical care systems are promoting the use of evidence-based guidelines that incorporate family history information to manage risk factors and treat heart disease. The following reports provide examples:

The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7)
Family history of premature cardiovascular disease (men under age 55 or women under age 65) is identified as a major risk factor for CVD.
http://www.nhlbi.nih.gov/guidelines/cholesterol/atp3_rpt.htm

The Third Report of the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III)
Family history should serve as a factor for making treatment decisions relative to setting and reaching LDL-cholesterol goals.
http://www.nhlbi.nih.gov/guidelines/cholesterol/atp3_rpt.htm.

American Heart Association Guidelines for Primary Prevention of Cardiovascular Disease and Stroke: 2002 Update
The guide calls for identifying high-risk patients for whom screening and intervention in first-degree relatives (including children) would be an important aspect of primary prevention.
http://circ.ahajournals.org/cgi/content/full/106/3/388

Conclusion

Mr. C already knows that because of his father's history, he needs to focus on actions to reduce his risk of CHD. Taking a more detailed family history of CHD and stroke could help Mr. C and his doctor discuss additional ways to reduce his risk. Mr. C didn't mention whether his father is the only relative with CHD or discuss his cholesterol level, except to say it was "a little high." Although inherited high-risk syndromes like familial hypercholesterolemia account for only a small proportion of CHD, failure to detect them

can have serious consequences for affected individuals and families.[7] A documented medical family history is valuable for distinguishing both moderate- and high-risk individuals and families.

References

1. CDC. Preventing Heart Disease and Stroke. Web site. Available at: http://www.cdc.gov/nccdphp/bb_heartdisease/index.htm. Accessed Feb 16, 2004.
2. Haga SB, Khoury MJ, Burke W. Genomic profiling to promote a healthy lifestyle: not ready for prime time. *Nature Genet* 2003;34:347-50.
3. Kardia SLR, Modell SM, Peyser PA. Family-centered approaches to understanding and preventing coronary heart disease. *Am J Prev Med* 2003;24:143-51.
4. Hunt SC, Gwinn M, Adams TD. Family history assessment: strategies for prevention of cardiovascular disease. *Am J Prev Med* 2003;24:136-42. Also available at: http://www.cdc.gov/genomics/info/reports/research/famhist_assess.htm. Accessed Feb 16, 2004.
5. CDC. Family History for Preventive Medicine and Public Health. Web site. Available at: http://www.cdc.gov/genomics/activities/famhx.htm. Accessed Feb 16, 2004.
6. Chronic Disease Summit. A report from the Association of State and Territorial Chronic Disease Directors. March 2002. Web site. Available at: http://www.chronicdisease.org/Genomics_Summit_Report.pdf. Accessed Feb 16, 2004.
7. Malarcher AM, Giles WH, Khoury MJ. Helping high-risk families: medical and public health approaches. *Genet Med* 2002;4:239-40. Also available at: http://www.cdc.gov/genomics/oldWeb01_16_04/info/reports/program/highriskfamily.htm. Accessed Feb 16, 2004.